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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte OLIVER HARNACK, WILLIAM E. FORD,
JURINA WESSELS, and AKIO YASUDA

Appeal 2009-007944¹
Application 10/631,351
Technology Center 1600

Decided: February 23, 2010

Before TONI R. SCHEINER, DONALD E. ADAMS, and LORA M. GREEN,
Administrative Patent Judges.

SCHEINER, *Administrative Patent Judge.*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 2-20, directed to attaching hydrophilic species to hydrophilic macromolecules immobilized on a hydrophobic surface. The claims have been rejected as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

¹ Heard February 2, 2010.

STATEMENT OF THE CASE

“[F]abrication of nano-devices . . . requires the specific assembly of molecules/macromolecules,” e.g., DNA, on a substrate (Spec. 2). Often, “it is desirable to have a hydrophobic surface as the substrate on which all further reactions are performed” (*id.*). In addition, “decoration of the assembled molecules/macromolecules by . . . metal nanoparticles, that confer specific qualities onto the molecular assemblies” (*id.*) without “non-selective binding of the species to the surface” (*id.*) is desirable.

Claim 2 is representative of the subject matter on appeal:

2. A method of attaching hydrophilic species to hydrophilic macromolecules immobilized on a hydrophobic surface, said method comprising the steps:

- (i) providing a hydrophobic surface,
- (ii) immobilizing hydrophilic macromolecules on the hydrophobic surface,
- (iii) exposing the hydrophilic macromolecules immobilized on the hydrophobic surface to hydrophilic species, whereby the hydrophilic species are attached to the hydrophilic macromolecules.

The Examiner relies on the following evidence:

Tajima	US 4,649,071	Mar. 10, 1987
Schuessler	US 2002/0050220 A1	May 2, 2002
Ford	US 2002/0065242 A1	May 30, 2002
Caldwell	US 5,516,703	May 14, 1996

D.E. Berning et al., *¹⁹⁸Au-Labeled Hydroxymethyl Phosphines as Models for Potential Therapeutic Pharmaceuticals*, 25 NUCLEAR MEDICINE & BIOLOGY 577-583 (1998).

D.C.G. Klein et al., *Ordered stretching of single molecules of deoxyribose nucleic acid between microfabricated polystyrene lines*, 78 APPLIED PHYSICS LETTERS 2396-2398 (2001).

In addition, Appellants rely on the following evidence:

Hongyou Fan and Gabriel P. Lopez, *Adsorption of Surface-Modified Colloidal Gold Particles onto Self-Assembled Monolayers: A Model System for the Study of Interactions of Colloidal Particles and Organic Surfaces*, 13 LANGMUIR 119-121 (1997).

The Examiner rejected the claims as follows:

- (A) Claims 2-11, 14-18, and 20 under 35 U.S.C. § 103(a), as unpatentable over Ford and Klein.
- (B) Claims 12 and 13 under 35 U.S.C. § 103(a) as unpatentable over Ford, Klein, and Tajima.
- (C) Claim 19 under 35 U.S.C. § 103(a) as unpatentable over Ford, Klein and Berning.
- (D) Claims 2-11, 14-16, and 20 under 35 U.S.C. § 103(a) as unpatentable over Ford and Schueller.
- (E) Claims 12 and 13 under 35 U.S.C. § 103(a) as unpatentable over Ford, Schueller, and Tajima.
- (F) Claim 19 under 35 U.S.C. § 103(a) as unpatentable over Ford, Schueller and Berning.
- (G) Claims 2-6, 11, 15, and 17-19, provisionally, under the doctrine of obviousness-type double patenting as unpatentable over claims 1-4, 14-16, and 20 of US Patent Application 09/990,049 in view of Caldwell.

OBVIOUSNESS: FORD AND KLEIN

Issue

There are three rejections of the claims premised in whole or in part on the Examiner's proposed combination of the teachings of Ford and Klein, and the underlying issue in all of these rejections is the same.

The Examiner finds that Ford describes immobilizing hydrophilic nucleic acids (i.e., hydrophilic macromolecules) on a surface, and exposing the immobilized nucleic acids to gold nanoparticles (i.e., a hydrophilic species). The Examiner acknowledges that Ford “fail[s] to teach the surface being hydrophobic” (Ans. 5), and cites Klein as disclosing nucleic acids immobilized on polystyrene in a “highly parallel” manner (*id.*). The Examiner concludes that it would have been obvious to attach Ford’s nucleic acids to a hydrophobic surface as taught by Klein “in order to provide an attachment method that is easy to employ and results in high yield” (*id.* at 5), since “[s]ince adsorption of a nanospecies to a substrate occurs whether the substrate is hydrophilic or hydrophobic” (*id.* at 12) and “the claims do not exclude adsorption of gold particles to the substrate” (*id.*).

Appellants contend that Fan provides evidence that “one of ordinary skill in the art would expect hydrophilic gold nanoparticles to adsorb non-specifically to a hydrophobic substrate” (App. Br. 7). Appellants contend that “[t]his non-specific reactivity would have dissuaded one of ordinary skill in the art from attempting to replace the hydrophilic substrate of Ford with the hydrophobic substrate of Klein” (*id.* at 8) because “[a] skilled artisan would expect that it would not be possible to confine the hydrophilic species to the locations of the immobilized macromolecule to create, e.g., nanowires, if a hydrophobic substrate were used in the process of Ford” (Reply Br. 2).

The issue raised by all three of these rejections is as follows: Has the Examiner established that one of ordinary skill in the art would have had a reason to replace Ford’s hydrophilic substrate with a hydrophobic substrate?

Findings of Fact

FF1 Ford discloses a “process for the direct and selective metallisation of nucleic acids via metal nanoparticles produced insitu which may be used, e.g., in the formation of nanowires, for electronic networks and circuits allowing a high density arrangement” (Ford ¶ 12).

FF2 Essentially, a platinum-DNA composite is applied to a polished silicon substrate and the substrate is de-salted with water, leaving elongated segments of DNA immobilized on the substrate. Then, gold nanoparticles are applied to the substrate, leaving “continuous metal [i.e., gold] coatings overlaying the elongated segments of DNA” (Ford ¶¶ 78, 79).

FF3 Ford teaches that “the surface of the silicon substrate [remains] relatively free of metal deposits, i.e., metallisation is mainly restricted to the DNA” (Ford ¶ 79).

FF4 Ford’s silicon substrate is not hydrophobic.

FF5 Klein discloses a molecular combing technique in which a silicon substrate is coated with a layer of polystyrene, and the coated substrate is dipped into a DNA/buffer solution. As the substrate is retracted from the DNA/buffer solution, “the ends of a DNA molecule preferentially bind to the polystyrene surface . . . presumably due either to an electrophilic addition of weak acids to alkenes, hydrophobic interaction, or to induced dipole-dipole interactions” (Klein 2396, col. 2 (internal citations omitted)). Klein teaches that this process “leads to uniformly stretched, parallel arrays of DNA molecules on the substrate surface” (*id.*).

FF6 Polystyrene is hydrophobic (Spec. 6, 9).

FF7 Fan, a reference cited by Appellants, describes the manner in which surface-modified colloidal gold particles having differing degrees of

hydrophobicity adsorb to gold surfaces also having differing degrees of hydrophobicity (Fan, Abstract).

FF8 According to Appellants, Fan demonstrates that “the more hydrophobic a surface is, the greater the adsorption of gold particles” and Fan’s “results confirm that the colloids studied adsorb from the aqueous solution more extensively to hydrophobic surfaces” (App. Br. 7).

FF9 The Examiner does not dispute Appellants’ interpretation of Fan’s teachings.

Principles of Law

An invention “composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. . . . [I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007).

“[A]ny need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed.” *KSR*, 550 U.S. at 420. However, “[w]e must still be careful not to allow hindsight reconstruction of references to reach the claimed invention without any explanation as to how or why the references would be combined to produce the claimed invention.” *Innogenetics, N.V. v. Abbott Labs.*, 512 F.3d 1363, 1374 n.3 (Fed. Cir. 2008).

Expectation of success is assessed from the perspective of a person of ordinary skill in the art, at the time the invention was made. *See Life Techs. Inc. v. Clontech Labs. Inc.*, 224 F.3d 1320, 1326 (Fed. Cir. 2000).

Analysis

Claim 2, which represents the invention in its most generic aspect, is directed to a method comprising immobilizing hydrophilic macromolecules on a hydrophobic surface, and exposing the immobilized hydrophilic macromolecules to a hydrophilic species, whereby the hydrophilic species are attached to the hydrophilic macromolecules. The Examiner finds that Ford immobilizes hydrophilic macromolecules (DNA) on a hydrophilic substrate, and then attaches a hydrophilic species (gold nanoparticles) to the immobilized DNA. Nevertheless, the Examiner concludes that it would have been obvious “to bind the hydrophilic macromolecules (DNA) to a hydrophobic substrate as taught by Klein . . . instead of a hydrophilic substrate” (Ans. 11), because Klein teaches that nucleic acids bind directly to polystyrene, a hydrophobic substrate (Ans. 5), “provid[ing] an attachment method that is easy to employ and results in high yield” (*id.*).

The Examiner acknowledges that Fan provides evidence that one of ordinary skill in the art would have expected that “adsorption of a nanospecies to a substrate occurs whether the substrate is hydrophilic or hydrophobic” (Ans. 12), but reasons that “one having ordinary skill would not be dissuaded from using a hydrophobic . . . substrate . . . since adsorption occurs with both substrates” (*id.*), and “the claims do not exclude adsorption of gold particles to the substrate” (*id.*).

It’s true that the claims don’t require selective attachment of the hydrophilic species to the hydrophilic macromolecules as opposed to the substrate. However, the relevant inquiry here is whether the Examiner has established that one of skill in the art would have had a reason to substitute a hydrophobic substrate for Ford’s hydrophilic substrate.

Klein teaches that DNA readily attaches to polystyrene, a hydrophobic substrate, and if Ford's objective was simply to bind DNA to a substrate, we would agree with the Examiner that it would have been obvious to substitute polystyrene for a hydrophilic substrate. However, Ford's objective is "direct and selective metallisation of nucleic acids via metal nanoparticles" in order to produce nanowires for electronic networks and circuits (FF1). Appellants contend that Fan provides evidence that one of skill in the art would have expected gold particles to readily bind a hydrophobic substrate (FF8). The Examiner doesn't dispute Appellants' interpretation of Fan's teachings (FF9), and agrees that one of skill in the art would have expected gold nanoparticles to bind directly to a hydrophobic substrate (Ans. 12). That being the case, the Examiner has not refuted Appellants' contention that it wouldn't have been obvious to substitute a hydrophobic substrate for Ford's hydrophilic substrate because one of skill in the art would have expected indiscriminant binding of nanoparticles to a hydrophobic substrate and DNA immobilized on the substrate to interfere with Ford's objective - producing nanowires by selective metallisation of the DNA bound to the substrate (FF1, FF3).

Conclusions of Law

The Examiner has not established that one of ordinary skill in the art would have had a reason to replace Ford's hydrophilic substrate with a hydrophobic substrate. Therefore, we are constrained to reverse the rejections of the claims based on Ford and Klein.

OBVIOUSNESS: FORD and SCHUELLER

Issue

There are three rejections of the claims premised in whole or in part on the Examiner's proposed combination of the teachings of Ford and Schueller, and the underlying issue in all of these rejections is the same.

The Examiner finds that Ford describes immobilizing hydrophilic nucleic acids (i.e., hydrophilic macromolecules) on a surface, and exposing the immobilized nucleic acids to gold nanoparticles (i.e., a hydrophilic species). The Examiner acknowledges that Ford "fail[s] to teach the surface being hydrophobic" (Ans. 7-8), and cites Schueller as disclosing biological molecules, including nucleic acids, stamped directly onto a polystyrene surface (*id.* at 8). The Examiner concludes that it would have been obvious to stamp Ford's nucleic acids onto a hydrophobic surface as taught by Schueller, "in order to provide a method for attachment of molecules that is more efficiently processed" (*id.*), since "[s]ince adsorption of a nanospecies to a substrate occurs whether the substrate is hydrophilic or hydrophobic" (*id.* at 12) and "the claims do not exclude adsorption of gold particles to the substrate" (*id.*).

Appellants contend that Fan provides evidence that "one of ordinary skill in the art would expect hydrophilic gold nanoparticles to adsorb non-specifically to a hydrophobic substrate" (App. Br. 7). Appellants contend that "one of ordinary skill in the art would not have expected that the method of Ford would function employing a hydrophobic substrate as disclosed in Schueller, for the reasons discussed above with respect to Ford and Klein" (*id.* at 11), because "[a] skilled artisan would expect that it would not be possible to confine the hydrophilic species to the locations of the

immobilized macromolecule to create, e.g., nanowires, if a hydrophobic substrate were used in the process of Ford” (Reply Br. 2).

The issue raised by all three of these rejections is as follows: Has the Examiner established that one of ordinary skill in the art would have had a reason to replace Ford’s hydrophilic substrate with a hydrophobic substrate?

Analysis

The rejections of the claims based on the Examiner’s proposed combination of Ford and Schueller suffer from the same infirmity as the rejections based on Ford and Klein, and Appellants’ arguments are equally applicable.

Conclusions of Law

The Examiner has not established that one of ordinary skill in the art would have had a reason to replace Ford’s hydrophilic substrate with a hydrophobic substrate. Therefore, we are constrained to reverse the rejections of the claims based on Ford and Schueller.

DOUBLE PATENTING

Appellants acknowledge that claims 2-6, 11, 15, and 17-19 stand provisionally rejected under the doctrine of obviousness-type double patenting as unpatentable over claims 1-4, 14-16, and 20 of US Application 09/990,049 in view of Caldwell, but “request[] that the double patenting rejection . . . be held in abeyance” (App. Br. 13).

However, in the absence of substantive arguments, we summarily affirm the provisional obviousness-type double patenting rejection.

SUMMARY

- (A) The rejection of claims 2-11, 14-18, and 20 under 35 U.S.C. § 103(a), as unpatentable over Ford and Klein is reversed.
- (B) The rejection of claims 12 and 13 under 35 U.S.C. § 103(a) as unpatentable over Ford, Klein, and Tajima is reversed.
- (C) The rejection of claim 19 under 35 U.S.C. § 103(a) as unpatentable over Ford, Klein and Berning is reversed.
- (D) The rejection of claims 2-11, 14-16, and 20 under 35 U.S.C. § 103(a) as unpatentable over Ford and Schueller is reversed.
- (E) The rejection of claims 12 and 13 under 35 U.S.C. § 103(a) as unpatentable over Ford, Schueller, and Tajima is reversed.
- (F) The rejection of claim 19 under 35 U.S.C. § 103(a) as unpatentable over Ford, Schueller and Berning is reversed.
- (G) The rejection of claims 2-6, 11, 15, and 17-19, provisionally, under the doctrine of obviousness-type double patenting as unpatentable over claims 1-4, 14-16, and 20 of US Patent Application 09/990,049 in view of Caldwell is affirmed.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv)(2006).

AFFIRMED-IN-PART

alw

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